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Platelet Rich Concentrates in Periodontal Regeneration

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Abstract

Platelet-rich concentrates (PRCs), such as platelet-rich plasma (PRP) and platelet-rich fibrin (PRF), are autologous preparations enriched with platelets, growth factors, and fibrin matrices that enhance periodontal wound healing and regeneration. Over time, newer generations including A-PRF, i-PRF, and T-PRF have been developed to improve biological activity and clinical outcomes. Evidence from randomized controlled trials and systematic reviews suggests that PRCs, when used alone or in combination with bone grafts and regenerative procedures, significantly improve probing depth reduction, clinical attachment level gain, bone fill, and soft-tissue healing compared with conventional therapies. Their advantages include biocompatibility, cost-effectiveness, and versatility in a wide range of periodontal applications. However, the lack of standardized preparation protocols, heterogeneity in clinical trials, and limited high-quality evidence for advanced formulations remain key limitations. Future research should focus on standardization, optimized formulations, and integration with bioactive materials to maximize regenerative potential.

Keywords: Leukocytes, Open-Flap Debridement, Platelet-Rich Concentrates, T-PRF

Introduction

Platelet-rich concentrates—including Platelet-Rich Plasma (PRP) and Platelet-Rich Fibrin (PRF)—are autologous biomaterials derived from a patient's blood, enriched with platelets, growth factors, leukocytes, and a supportive fibrin matrix. These materials have emerged as promising adjuncts in periodontal therapy because they can enhance wound healing, stimulate tissue regeneration, and act as scaffolds facilitating cellular proliferation and differentiation.

1. Composition & Biological Mechanism

PRF is a second-generation platelet concentrate featuring a fibrin matrix that captures platelets and leukocytes, allowing for sustained release of biologically active growth factors like PDGF, TGF-β, and VEGF. This scaffold facilitates coordinated tissue healing through both structural and cellular signaling benefits.

2. Preclinical and Biomolecular Evidence

In animal and in vitro models, PRF has demonstrated significant promotion of osteogenic activities. For instance, a study combining PRF with rat periodontal ligament stem cells showed increased expression of BSP, osteocalcin, and RUNX2, along with enhanced new bone formation in defect models.[1]

A study using alveolar bone progenitors showed that PRF led to a 3.6-fold increase in the early osteoblast transcription factor RUNX2 and reduced expression of mineralization inhibitor MGP, suggesting superior osteogenic support. Clinically, this correlated with approximately 5 mm of alveolar bone height gain and improved soft tissue healing.[2]

3. Clinical Evidence in Periodontal Defects

Randomized Controlled Trials (RCTs): An RCT comparing PRF, PRP, and open-flap debridement (OFD) in intrabony defects found that both PRF and PRP yielded significantly better probing depth (PD) reduction, clinical attachment level (CAL) gain, and bone fill (~55%) than OFD alone. PRF was noted for being less time-consuming and technique-sensitive than PRP.[3]

Another controlled clinical study (2025) showed that combining PRF with OFD resulted in greater bone fill (45% vs. 30%), alongside deeper clinical improvements in PD and CAL, when compared to OFD alone.[4]

In 2025, an RCT evaluating PRF with bone grafts reported improved outcomes over graft alone: PD reduction of ~4.2 mm vs. 3.0 mm, CAL gain of 3.5 mm vs. 2.6 mm, and bone fill of 68% vs. 45%.[5]

A split-mouth study (2017) monitored growth factor levels in gingival crevicular fluid post-treatment. Sites treated with PRF and OFD exhibited significantly higher levels of FGF-2, TGF-β1, and PDGF-BB at 2 and 4 weeks, alongside improved PD reduction and relative CAL gain.[6]

Classification Of Platelet Rich Concentrates

1. Four-Category System Based on Leukocyte & Fibrin Content

A widely accepted classification—rooted in consensus and clarity divides PRCs into four principal types defined by leukocyte presence and fibrin architecture:

Category	Description	Examples
P-PRP (Pure Platelet-Rich Plasma)	Leukocyte-poor, low-density fibrin network; available in liquid form or activated gel.	Cell separator PRP, Vivostat PRF (misnomer), Anitua's PRGF
L-PRP (Leukocyte- & Platelet-Rich Plasma)	Contains leukocytes, low-density fibrin; one-step centrifugation protocols.	Curasan, Regen, GPS PRP, Biomet GPS system
P-PRF (Pure Platelet-Rich Fibrin)	Leukocyte-poor, dense fibrin clot; no anticoagulants or activators needed.	Fibrinet
L-PRF (Leukocyte- & Platelet-Rich Fibrin)	Contains leukocytes, dense fibrin matrix; second-generation PRF (e.g., Choukroun's PRF).	Choukroun's PRF

This schema is endorsed by Dohan-Ehrenfest and colleagues (2009), with further elaboration in consensus articles.[7]

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2. Generational Evolution of PRCs

The classification also reflects a generational progression in platelet concentrate evolution:

- First Generation: PRP (P-PRP and L-PRP) – available as liquid or activated gel; rapid but short-lived release of growth factors.
- Second Generation: PRF (P-PRF and L-PRF) – presents in a fibrin clot form, naturally polymerized without chemical additives; sustained growth factor releases over ~7 days.[8]

3. Third-Generation Platelet Concentrates — Advanced Modifications

More recent refinements—termed "third generation" PRCs—augment biological properties via altered centrifugation or materials:

- A-PRF (Advanced PRF): Prepared using low-speed centrifugation (LSCC) (reduced RCF ~208 g), yielding a porous clot rich in neutrophils and growth factor potential.
- A-PRF+: Variant with optimized settings for higher growth factor yield through greater leukocyte inclusion.
- i-PRF (Injectable PRF): Liquid form, achieved via ultra-rapid centrifugation (~700 g for ~3 minutes), enabling injectability and convenience.
- T-PRF (Titanium-prepared PRF): Clot formed using titanium tubes at ~2800 rpm for ~12 min; yields more densely polymerized fibrin due to better hemocompatibility of titanium.[9]

Other noted innovations include:

- CGF (Concentrated Growth Factor): Fibrin tissue adhesive offering hemostasias, improved graft stability, and antimicrobial effects, proposed around 2006.[10]
- Alb-PRF and Lyophilized PRF: Experimental forms designed for enhanced handling and biological release profiles.[11]

Preparation Protocols

Core PRF Protocols (no anticoagulant)

1. L-PRF (Choukroun's "classic" PRF, solid clot/membrane)

- Blood draw: 9–10 mL whole blood into plain glass/silica-coated tubes (no anticoagulant). Start centrifugation immediately (<60–120 s) to avoid premature clotting.[12]
- Centrifugation (typical original settings): ~2700 rpm for 12 min (≈~400–650 g depending on rotor). Variants widely reported as 3000 rpm × 10 min. [13]
- Harvest: Remove the middle fibrin clot, separate from RBC layer, and press gently between sterile gauze/PRF box to form a membrane. [14]

  Notes: Simplicity, no additives; sustained growth-factor release over days. [15]

2. A-PRF / A-PRF+ (low-speed concept, solid clot/membrane)

- Blood draw: Plain glass tubes, no anticoagulant. Spin immediately.
- Centrifugation (commonly reported):
- A-PRF: ~1500 rpm for 14 min (≈~200–230 g on Process/Duo centrifuges). [16]
- A-PRF+: ~1300–1500 rpm for 8 min (≈~200 g), device-specific. [17]
- Harvest/Use: As for L-PRF (clot → membrane). Lower g-forces increase leukocyte capture and porosity. [18]

3. i-PRF (injectable PRF, liquid)

- Blood draw: Plastic (non-activating) tubes without anticoagulant to delay clotting long enough to obtain a liquid fraction. [19]

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- Centrifugation (typical early reports): ~700 rpm for 3 min (very low g, short time) to keep PRF liquid for immediate injection/mixing. (Exact g depends on rotor; many devices target ~60–200 g for 3–4 min.).[20]
- Use window: Inject/mix with biomaterials within minutes before it polymerizes.[21]

4. T-PRF (titanium-prepared PRF, solid)

- Blood draw: Titanium tubes (medical-grade), no anticoagulant. Rationale: titanium's hemocompatibility may enhance fibrin polymerization.
- Centrifugation: Reported protocols mirror L-PRF timeframes (e.g., ~2700–3000 rpm for ~10–12 min; device-dependent). Produces a denser fibrin network.
- Harvest/Use: As for L-PRF (clot → membrane).[22]

5. CGF (Concentrated Growth Factor, solid/membrane)

- Blood draw: No anticoagulant, Medifuge/Silfradent-type centrifuges with programmed, alternating speeds (proprietary sequence).
- Centrifugation: Variable/stepped speeds per device to yield a thicker, denser fibrin matrix than standard PRF. (Manufacturers publish exact step profiles; literature consistently stresses alternating controlled speeds rather than a single RPM.).[23]
- Harvest/Use: Collect the CGF clot and compress as needed.[24]

PRP Protocols (with anticoagulant; liquid/gel)

6. P-PRP (PRGF-Endoret® style; leukocyte-poor PRP)

- Blood draw: Tubes preloaded with trisodium citrate (e.g., 0.4–0.9 mL depending on version) as anticoagulant.[25]
- Centrifugation: Single spin per Endured methodology (device-specified RCF/time) to stratify plasma into fractions (F1/F2, etc.).[26]
- Activation (to make gel or membrane): Add calcium chloride (e.g., ~20–50 µL per mL PRGF; protocol updates exist) and incubate at ~37 °C for ~20–60 min, then use as gel or cast membrane.[27]

7. L-PRP (leukocyte-rich PRP; "double-spin")

- Blood draw: Citrate anticoagulant tubes.[28]
- Centrifugation (generalizable framework):

1) Soft spin (≈100–300 g for 5–10 min) → transfer plasma + buffy coat.
2) Hard spin (≈400–2000 g for 5–10 min) → pellet platelets; resuspend in minimal plasma. Include buffy coat to retain leukocytes (L-PRP) or avoid it for P-PRP.[29]

- Activation (optional): Calcium chloride/thrombin as required for gel formation. Report if used.[30]

Clinical Application in Periodontology

1. Treatment of intrabony (vertical) periodontal defects

What clinicians do:

PRF/PRP (alone or combined with bone grafts/xenografts/EMD) is placed inside intrabony defects after open-flap debridement to promote bone fill and clinical attachment gain.

- Evidence:

Multiple systematic reviews and recent meta-analyses show PRF significantly improves probing depth (PD) reduction, clinical attachment level (CAL) gain, and radiographic bone fill versus OFD (and often adds benefit when combined with grafts).[31]

- Practical note: Combining PRF/i-PRF with bone grafts (sticky bone, graft + i-PRF) often improves graft handling and bone fill.[32]

2. Furcation defects

What clinicians do:

PRF used as an adjunct to flap surgery or regenerative grafting in Class II furcation defects.

- Evidence:

Recent RCTs and systematic reviews support PRF's positive impact on horizontal/vertical bone fill and

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clinical improvement in furcation sites compared to conventional modalities.[33]

3. Gingival recession / periodontal plastic surgery (root coverage)

What clinicians do:

PRF membranes (L-PRF, A-PRF) are used alone or combined with coronally advanced flaps (CAF) or connective tissue grafts to promote root coverage and soft-tissue healing.

- Evidence:

Reviews report improved soft-tissue healing, faster re-epithelialization, and comparable root coverage to conventional grafts in select studies — PRF is particularly attractive where donor-site morbidity is a concern.[34]

4. Alveolar ridge preservation / Guided bone regeneration (GBR) / Ridge augmentation

What clinicians do:

PRF is used as a biologic membrane, mixed with bone grafts, or applied to sockets to preserve ridge width and reduce graft resorption.

- Evidence:

Meta-analyses indicate PRF use is associated with improved horizontal ridge width and reduced graft resorption in ARR/GBR procedures, and can enhance soft-tissue healing.[35]

5. Socket preservation / Implant site development / Sinus augmentation

What clinicians do:

PRF or PRP added to sockets or graft materials to accelerate healing, improve bone density, and reduce post-operative pain.

- Evidence:

Clinical trials show faster soft-tissue healing and sometimes higher early bone density when PRF/T-PRF is used; evidence for long-term implant success is promising but limited. T-PRF has shown improved early bone density and ridge preservation in recent trials.[36]

6. Adjunct to non-surgical periodontal therapy (NSPT) and use in medically compromised patients

What clinicians do:

i-PRF or repeated PRF injections are used with scaling & root planing (SRP) to boost pocket healing, especially in deep pockets, smokers, or difficult cases.

- Evidence:

RCTs and systematic reviews indicate i-PRF as an adjunct to SRP can yield greater PD reduction and CAL gain (including evidence in smokers), and increases local growth factor levels in GCF.[37]

7. Treatment of combined therapy scenarios and biomodified PRF

What clinicians do:

PRF is combined with grafts, antimicrobials (e.g., metronidazole-infused PRF), or used to make “sticky bone” (graft + i-PRF) to improve handling and biological activity.

- Evidence:

Trials support sticky bone and CGF combinations producing favorable defect fill and handling characteristics; newer dual-action and drug-infused PRF approaches are under clinical evaluation.[39]

8. Specialized PRF variants: T-PRF, A-PRF+, CGF, e-PRF — practical impact

- T-PRF (titanium prepared PRF): Reported to create a denser fibrin network with higher growth-factor retention — clinical meta-analyses support its benefit in hard/soft tissue correction and ridge preservation.
- A-PRF / A-PRF+ and i-PRF: Low-speed centrifugation variants that increase leukocyte and growth-factor content and/or enable injectability — several clinical studies and reviews show favorable periodontal healing outcomes.[40]

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- CGF / Sticky bone: Device-programmed centrifugation yields a dense matrix used successfully in intrabony defects and graft stabilization.[41]

Practical recommendations for clinicians (based on current literature)

1. Match PRC type to clinical need: Use solid PRF membranes for membranes/soft-tissue augmentation and intrabony defects; use i-PRF when injectability or mixing with grafts is required.[42]
2. Report preparation details: Always report tube type, RCF/g-force, centrifuge rotor radius, and time to centrifugation in studies to allow reproducibility. (Widely emphasized across reviews.)[43]
3. Consider combinations: For deep intrabony defects, combine PRF with bone grafts or EMD for improved outcomes; sticky bone (graft + i-PRF) improves handling and stability.[44]
4. Use cautiously in compromised patients: Emerging evidence supports i-PRF adjuncts in smokers and medically compromised patients, but tailor expectations and monitor outcomes closely.[45]

Advantages of Platelet Rich Concentrates

1. Deliver a concentrated cocktail of growth factors that stimulate healing — platelet concentrates release PDGF, TGF-β, VEGF, IGF and other mediators that promote chemotaxis, cell proliferation and angiogenesis (mechanism supporting regeneration).[46]
2. Improve clinical outcomes (CAL gain & PPD reduction) when used as an adjunct — systematic reviews and meta-analyses report greater clinical attachment level gains and probing pocket depth reductions in intrabony defects and some furcation defects when PRF/PRP are added to conventional surgery vs surgery alone. (Effect size varies by study and PRC type.)
3. Enhance bone fill / radiographic bone regeneration many RCTs and pooled analyses show more bone fill in intrabony defects when platelet concentrates are used, particularly when combined with bone grafts or as a graft stabilizer.[47]
4. Better soft-tissue healing, wound sealing and reduced postoperative morbidity — PRF in particular (because of its fibrin matrix) supports clot stability, epithelial migration and wound sealing, and several studies report reduced pain, swelling and faster soft tissue closure.[48]
5. Sustained release profiles with newer forms (A-PRF, i-PRF, T-PRF) — advanced and injectable PRF preparations show more prolonged growth-factor release and improved cell migration in vitro and promising clinical signals (useful for sustained regenerative stimulus).[49]
6. Autologous and low immunogenicity / low cost and chairside preparation — since platelet concentrates are prepared from the patient's own blood, they avoid donor immunogenicity and infectious-disease risks associated with allografts; preparation is generally simple and inexpensive relative to some biomaterials. [50]
7. Versatility — can be used alone or combined with graft materials / membranes —clinicians use PCs for intrabony defects, furcations, ridge preservation, sinus lifts and soft-tissue grafting as an adjunct to improve handling and biological activity. [51]

Limitations of Platelet Rich Concentrates

1. Lack of Standardization in Preparation and Terminology

- There's considerable heterogeneity in PRP/PRF formulations— different devices, centrifugation parameters, platelet yields, purity, and activation methods lead to inconsistent products

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- Protocols are frequently incompletely reported, with many studies failing to specify critical aspects like activation agents, temperature control, or platelet content.
- Terminology varies across studies—many use the umbrella term "PRP" without clarifying the exact type or formulation.

2. Variability in Clinical Protocols

- There is wide variation in preparation devices (e.g., gravitational vs continuous centrifuges), affecting platelet yield, viability, contamination, and outcomes.
- Activation methods—with thrombin, calcium chloride, or none—are underreported, which hampers reproducibility and outcome comparison.
- Temperature control, which influences platelet viability, is often omitted from reporting—only about 25% of studies mention maintaining temperature during preparation.

3. Quality Control and Performance Bias

- Most PRP/PRF products are prepared "home-made" without standardized quality controls, leading to performance bias in clinical trials
- Many randomized controlled trials (RCTs) are empirically designed, lack rigorous methodology, or suffer from small sample sizes, limiting reliability.
- Publication bias, cognitive bias, and selective reporting pose additional challenges in interpreting meta-analyses based on such studies. [52]

4. Clinical Efficacy Evidence is mixed/weak

- Meta-analyses report limited or conflicting evidence regarding PRP's efficacy across orthopedics, oral surgery, and dermatology.
- In orthopedics, evidence shows minimal benefit in musculoskeletal injuries, while for osteoarthritis, results are tentative but not definitive.
- Dental and gynecological applications suffer from a low quality of RCTs and high risk of bias.
- Advanced formulations like i-PRF and A-PRF are newer and lack sufficient clinical validation or high-quality evidence.

5. Technical and Practical Constraints

- The complexity of preparation—requiring quick and sterile handling, precise centrifugation, and skilled operators—raises the potential for contamination and inconsistent quality.
- Many studies omit key details such as PRP concentration, activation protocol, temperature control, or sterility measures, limiting reproducibility and clinical translation.
- There may also be immune risks—for example, antibodies formed against bovine factor Va (from bovine thrombin use) could, in rare cases, cause coagulation issues.

Current Evidence

1. Intrabony defects (periodontal bone defects)

- Multiple systematic reviews and a 2024 network meta-analysis report that PRF used as an adjunct to surgical regenerative procedures produces greater CAL gain, greater PPD reduction, and improved bone fill versus conventional therapy alone in many trials. Effect sizes are generally modest-to-moderate, and heterogeneity across trials is substantial.[53]

2. Root coverage / soft-tissue periodontal plastic surgery

- For root coverage with coronally advanced flap procedures, PRF added to the flap often improves amount of root coverage and early soft tissue healing, although outcomes depend on baseline tissue phenotype and whether PRF is used alone or with grafts.[54]

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3. Furcation defects & complex sites

- Emerging RCTs and pooled analyses indicate PRF can improve outcomes in class II furcation defects and certain complex sites, but evidence is smaller in quantity and lower in quality compared with intrabony defect literature. [55]

4. Variants (i-PRF, T-PRF, A-PRF, titanium-PRF)

- Laboratory/biologic data show newer variants (injectable PRF, advanced PRF forms, titanium-prepared PRF) have altered release kinetics of growth factors and favourable cell responses; systematic reviews/meta-analyses show promising clinical signals but insufficient high-quality head-to-head RCTs to claim superiority over standard PRF[56]

5. Alveolar ridge preservation / socket healing / implant site development

- PRF/PRP used for ridge preservation and socket healing frequently reduces early postoperative morbidity and may preserve ridge dimensions better than spontaneous healing; bone regeneration benefits versus bone grafts are variable. Newer trials (including 2024 2025) continue to explore T-PRF and combination approaches

6. Safety

- Because concentrates are autologous, serious adverse events are rare in published trials; however, adverse event (AE) reporting is inconsistent across studies, limiting robust safety meta-estimates.[57]

Practical clinical takeaway

- Use PRF as an adjunct in intrabony defect surgery and in certain root coverage procedures when you want to improve early healing and modestly increase CAL/PPD outcomes—expect improvements over standard therapy but manage expectations about magnitude and durability.[58]
- Document your PRF/PRP preparation parameters (centrifuge model, RPM/g-force, time, tube type, whether activated) and clinical protocol clearly—this improves reproducibility and helps interpret outcomes.[59]
- For novel variants (i-PRF, T-PRF), view them as promising but still investigational relative to standard PRF until more high-quality comparative RCTs are available.[60]

Future Directions and Innovation

1. Standardization, classification and quality control (foundational).
2. Optimized/next-gen PRF formulations (i-PRF, A-PRF, T-PRF and beyond).[61]
3. Cellular therapies + PRF (PDLSCs, ASCs, GMSCs).[62]
4. Bioactive scaffolds, composites & hierarchical architectures.[63]
5. Controlled / sustained release and nano-delivery systems.[64]
6. 3D bioprinting & personalized defect-matched constructs.
7. PRF-derived cell-free products: exosomes & secretome therapies.
8. Combination biologics & adjuncts (PRF + growth factors, small molecules, retinoids, biomimetics).
9. Biomarkers, imaging, and precision treatment selection.[65]
10. Clinical evidence infrastructure: harmonized outcomes, registries & larger RCTs.

Conclusion

Platelet-rich concentrates (PRP, PRF, and their advanced derivatives) represent a significant advancement in periodontal regenerative therapy. By providing a concentrated source of platelets, growth factors, and a natural fibrin scaffold, they enhance wound healing,

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promote bone and soft tissue regeneration, and improve clinical outcomes in intrabony defects, furcations, root coverage, ridge preservation, and implant site development. Their autologous nature ensures biocompatibility, cost-effectiveness, and minimal risk of immunogenic reactions.

However, limitations such as lack of standardization in preparation, variability in clinical protocols, and insufficient high-quality randomized controlled trials still restrict their universal application. Current evidence supports PRF, especially in intrabony defects and soft tissue procedures, as a reliable adjunct to conventional therapies, while newer formulations like A-PRF, i-PRF, and T-PRF show promising but still evolving potential.

Future directions lie in protocol standardization, integration with biomaterials, controlled release systems, and next-generation biologics, aiming to maximize regenerative outcomes and establish PRCs as a mainstream tool in periodontal therapy

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